Landes Bioscience www.landesbioscience.com

Supplemental Material to:

Ester Hernández, Rafael Bargiela, María Suárez Diez, Anette Friedrichs, Ana Elena Pérez-Cobas, María José Gosalbes, Henrik Knecht, Mónica Martínez-Martínez, Jana Seifert Martin von Bergen Alejandro Artacho, Alicia Ruiz, Cristina Campoy, Amparo Latorre, Stephan J Ott, Andrés Moya, Antonio Suárez, Vitor A.P. Martins dos Santos and Manuel Ferrer

Functional consequences of microbial shifts in the human gastrointestinal tract linked to antibiotic treatment and obesity

Gut Microbes 2013; 4(4)
http://dx.doi.org/10.4161/gmic.25321

http://www.landesbioscience.com/journals/gutmicrobes/article/25321/

Supplementary Files

Supplementary File includes:

Supplementary Figures S1 to S3

Supplementary Tables S1 to S5

Supplementary Figures

Figure S1. Relative contribution of the abundance level of glycoside-hydrolase like enzyme recovered from each of the shotgun metaproteomes of one patient (P1) receiving β-lactam therapy. The abundance values of GH-like enzymes (183 in total), from a total number of 3,011 proteins that were unambiguously quantified in the same set of samples used for activity tests, were considered: FS-0, 211; FS-3, 186; FS-6, 188; FS-11, 158; and FS-14, 199. Abbreviations as follows: GHx, family of Glycoside-Hydrolases; CBM, Carbohydrate-Binding Module. Results are the average of two independent technical replicates per sample and graphs was plotted using mean values with the standard deviation lower than 2%. Note: Predicted GH-like enzymes and CBMs were identified (and manually analyzed) in the shotgun metaproteomes via the Basic Local Alignment Search Tool Protein (BLASTP) analysis against the Carbohydrate Active Enzyme database,[23] according to an E-value <e^{-05} and a sequence homology ≥50%.

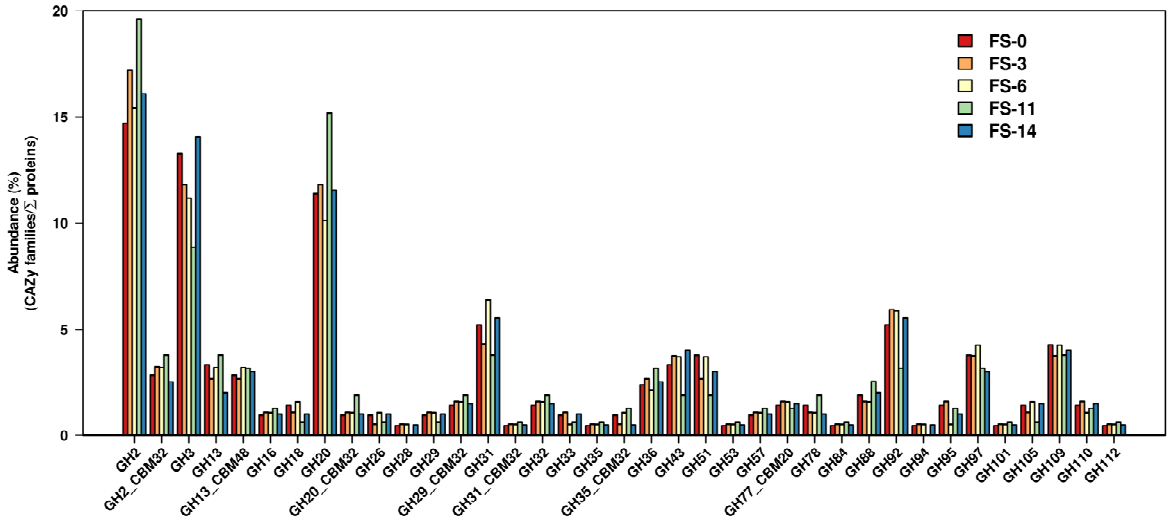


Figure S2. Antibiotic-mediated community behavior characterized by mapping to metabolic pathways. Proteome-scale metabolic reconstructions were based on the expression values of a set of proteins with Enzyme Commission (EC) number that were found among the 3,011 proteins that were unambiguously quantified in the metaproteomes of all the P1 samples (receiving β-lactam therapy).[10] Ad-hoc computer programs written in C and Perl were used to obtain information from local copies of KEGG and to generate the graphical representations. The following color code was used: green, increased expression; red, decreased expression and thickness was proportional to the ratio. Maps were generated based on the expression level of proteins found in samples FS-3 (A), FS-6 (B), FS-11 (C) and FS-14 (D) compared to the values in FS-0. This Figure is provided as separate file (escalable PDF version) to ensure high quality resolution.

Figure S3. Obesity-mediated community behavior characterized by mapping to metabolic pathways. Proteome-scale metabolic reconstructions were based on the expression values of a set of proteins with Enzyme Commission (EC) number that were found among the 613 proteins that were unambiguously quantified in the metaproteomes of one obese adolescent (Obese111) and one lean adolescent (LeanCE01).[6] Ad-hoc computer programs written in C and Perl were used to obtain information from local copies of KEGG and to generate the graphical representations. The following color code was used: green, increased expression; red, decreased expression and thickness was proportional to the ratio. Maps were generated based on the expression level of proteins found in obese compared to the values in lean. This Figure is provided as separate file (escalable PDF version) to ensure high quality resolution.

Supplementary Tables

Table S1 Biochemical measures and general characteristics of antibiotic-treated patients as well as obese and lean individuals investigated in the present study.

Sample[1]	Age	Sex[2]	Weight (kg)	Height (cm)	BMI (kg/m2)	Fasting glucose (mg/dL)	Fasting insulin (pg/mL)	HOMA-IR[3]	Uric acid (mg/dL)	Total cholesterol (mg/dL)	HDL cholesterol (mg/dL)	LDL cholesterol (mg/dL)	Tryglicerides (mg/dL)
Obese110	13	M	66.2	161.6	25.35	82	14.9	0.07	5.4	118	51	47	100
Obese111	15	M	102.7	171	35.12	80	17.5	0.09	8.6	198	46	118	172
Obese116	16	F	85.95	165.8	31.27	83	13.7	0.07	5.3	131	49	70	59
Obese122	14	M	108.2	181.5	32.85	86	30.9	0.16	8.1	139	50	77	59
Obese125	16	F	74.2	173	24.79	83	9.2	0.05	4.5	147	66	68	67
Obese128	14	F	71.6	165.5	26.14	79	12	0.06	6.3	119	43	66	48
Obese129	15	M	100.2	174	33.1	84	23.1	0.12	6.5	197	45	120	160
LeanCE01	15	F	63.1	165	23.18	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
LeanCE03	13	M	40.9	151	17.94	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
LeanCE05	16	F	61.5	162	23.43	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
LeanCE07	16	F	58.1	157	23.57	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
LeanCE09	15	M	65.9	173	22.02	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
P1	68	M	105	177	33.5	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
P2	73	F	54.0	156	22.20	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

[1]Note: Biochemical measures and general characteristics of individuals P1, P2, Obese111 and leanCE01 have been previously described; for details see ref. 6 and 10 (main text).
[2]Abbreviations as follows: M, male; F, female
[3]HOMA-IR index was calculated using a free web HOMA-IR calculator available at http://www.hcvsociety.org/files/HOMACalc.htm
n.a. Data not available.

Table S2 Differences in the relative contribution of carbohydrate turnovers. Combine shifts during the antibiotic treatment as compared to the admission day and shifts between obese and lean subjects are specifically indicated. The relative activity level was calculated per each sample according to the data provided in Fig. 1 and mean values from three independent measurements per group of samples are given.

Sugar substrate	**Relative contribution (%) of glycosidase activities referred to the total**[1]						
	FS-0 (n=2)	FS-3 (n=2)	FS-6 (n=2)	FS-11 (n=2)	FS-14 (n=2)	Obese (n=7)	Lean (n=5)
α-Glucose	4.96	2.11	2.90	0.42	3.06	7.76	1.40
β-D-Glucose	3.61	1.63	3.78	6.14	5.73	7.33	4.94
α-Maltose	2.89	1.10	1.53	2.08	1.83	4.63	7.85
α-D-Maltopentose	2.60	1.21	1.20	0.87	1.15	2.87	4.71
α-D-Maltohexose	5.89	1.72	2.24	4.47	2.75	2.87	4.47
β-D-Cellobiose	0.19	0.17	0.24	0.13	0.19	2.05	4.27
α-L-Galactose	13.64	26.12	15.60	16.54	17.59	19.72	18.48
β-D-Galactose	39.52	55.60	49.54	31.08	47.57	19.50	13.70
α-Xylose	1.06	0.22	0.26	0.13	0.23	0.55	0.64
β-Xylose	0.34	0.28	2.21	0.17	0.39	5.69	9.47
α-Arabinopyranose	4.27	2.54	4.23	4.77	5.48	1.26	4.03
β-Arabinopyranose	0.34	0.16	0.15	0.11	0.19	0.48	0.43
α-Arabinofuranose	2.84	2.09	3.52	1.61	2.19	11.03	1.07
α-L-Rhamnose	0.88	0.62	2.32	1.89	0.67	1.59	4.24
α-Mannose	11.91	1.49	3.10	11.33	4.37	2.86	2.86
β-D-Mannose	0.77	0.12	0.41	0.42	0.54	0.53	0.93
β-Lactose	1.25	1.21	1.46	1.95	2.62	6.43	8.22
α-Fucose	0.24	0.19	0.64	0.21	0.17	1.15	1.94
β-Fucose	2.10	1.88	2.36	3.41	3.13	1.11	5.26
β-Glucuronide	0.08	0.02	0.13	0.08	0.07	0.34	0.24
β-Acetylglucuronide	0.11	0.05	0.13	0.06	0.06	0.23	0.30
α-Acetylneuraminic acid	0.24	0.04	1.23	5.58	0.01	0.01	0.26
β-N-Acetyl-β-D-glucosaminide	0.28	0.05	0.80	6.55	0.02	0.02	0.32

[1]Standard deviation (SD) ranging (refer to the relative contribution [%]) from 0.33 to 1.69×10^{-5} (for FS-0; n=2, three replicates each), 0.21 to 7.7×10^{-5} (for FS-3; n=2, three replicates each), 0.30 to 1.3×10^{-4} (for FS-6; n=2, three replicates each), 0.25 to 2.9×10^{-5} (for FS-11; n=2, three replicates each), 0.43 to 1.8×10^{-5} (for FS-14; n=2, three replicates each), 1.0 to 8.0×10^{-4} (for obese; n=5, three replicates each) and 1.0 to 0.0023 (for lean; n=7, three replicates each).

Table S3. Proteomic-based responses to KEGG reactions during the 14-days β-lactam therapy of P1. A detailed analysis of the KEGG reactions found to be differentially activated or deactivated and appearing or disappearing as compared to the sample before the beginning of the therapy (day 0), on relative concentration of protein basis, is specifically shown. Fold changes (FC), calculated as the average of protein expression levels of proteins assigned to the same reaction in samples FS-3, FS-6, FS-11 and FS-14 as compared to FS-0, are also provided. Note: the terms "activated" and "deactivated" refer to the number of metabolic reactions that were up- or down-regulated, respectively, by considering a threshold of at least 1.5 fold change in abundance levels of the corresponding pooled proteins belonging to a particular reaction, as compared with the initial sample (day 0); the term "new" refers to the number of reactions containing proteins that were only expressed in samples FS-3 to FS-14 as compared to FS-0; the term "disappear" refers to the number of reactions containing proteins that were only expressed in samples FS-0 as compared to FS-3 to FS-14.

t (days)	**Number of reactions**		**Number of activated/deactivated reactions according to fold changes (FC) groups**				
	Activated	**New**	**1.5<FC<5**	**5≤FC<10**	**10≤FC<15**	**15≤FC<20**	**20≤FC**
FS-3	116	12	65	19	6	1	13
FS-6	90	11	39	20	4	3	13
FS-11	47	7	29	3	3	1	4
FS-14	93	11	57	12	4	0	9
	Deactivated	**Disappear**	**1.5 <1/FC<5**	**5 ≤1/FC<10**	**10 ≤1/FC<15**	**15 ≤1/FC<20**	**20 ≤1/FC**
FS-3	50	8	26	7	2	1	6
FS-6	63	1	43	8	2	5	4
FS-11	121	20	40	18	7	7	29
FS-14	61	3	38	11	5	2	2

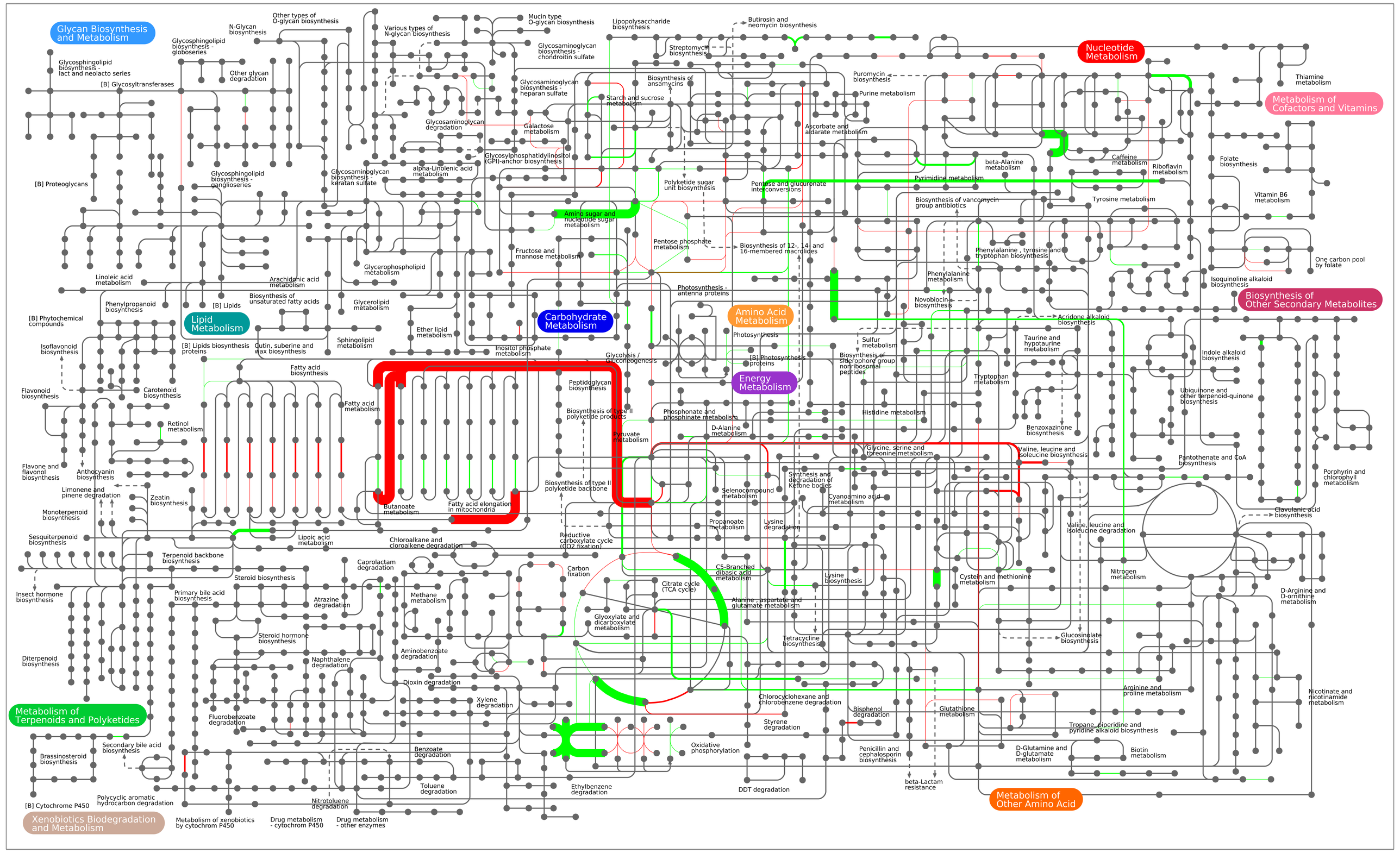
Table S4. Proteomic-based responses to KEGG pathways during the 14-days β-lactam therapy of P1. The changes in the number of pathways were computed as a function of the number of up- and down-regulated reactions in each pathway, by considering a threshold of at least 1.5 fold changes in abundance levels of the corresponding pooled proteins. The table presents the differences between the number of up- and down-regulated reactions, therefore a positive number is interpreted as a signal of pathway upregulation, whereas a negative number indicates and overall pathway down-regulation. For additional quantification of selected pathways see Table S5.

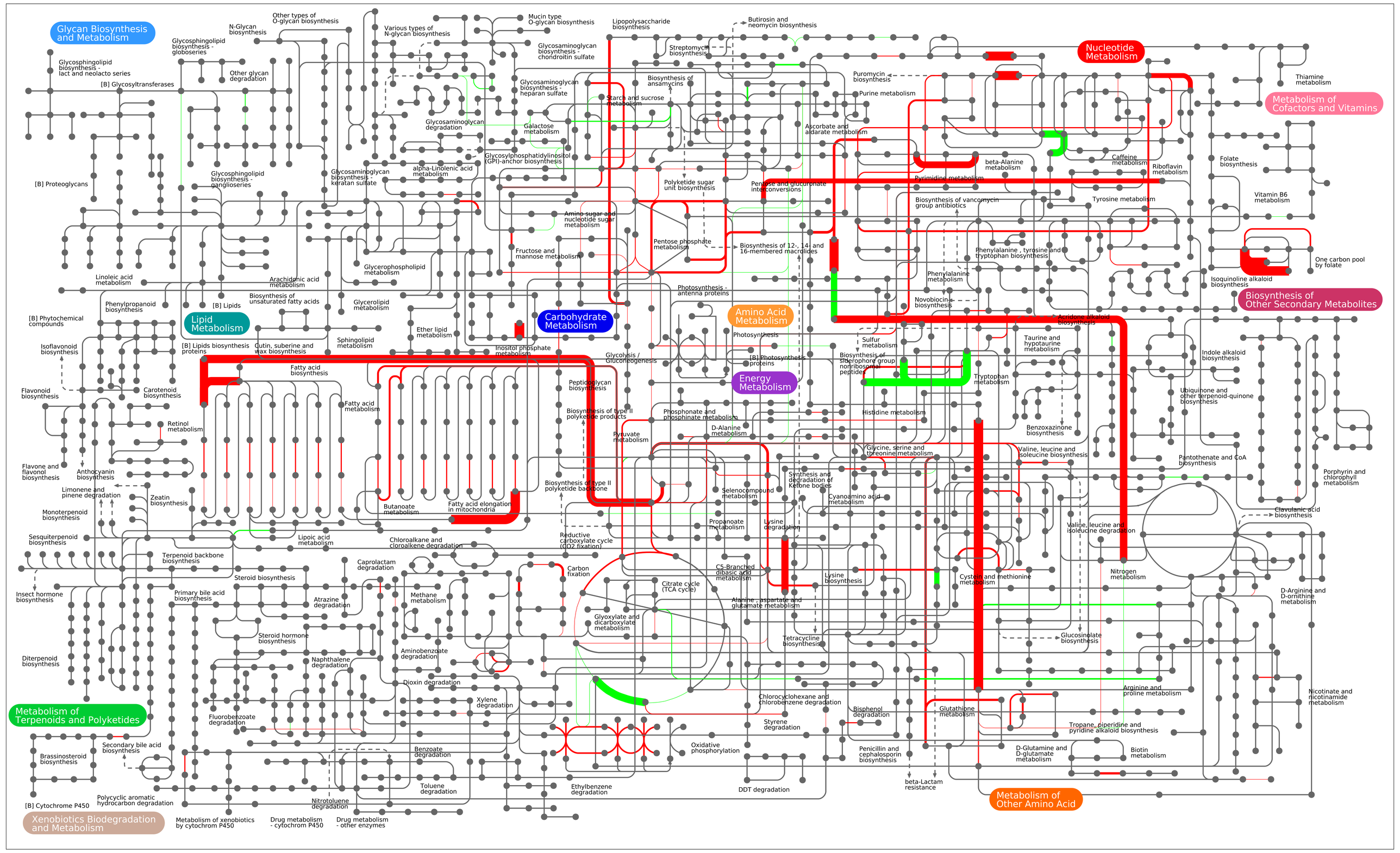
KEGG pathway	Kegg ID	FS-3	FS-6	FS-11	FS-14
Glycolysis / Gluconeogenesis	ec00010	0	-1	-9	0
Citrate cycle (TCA cycle)	ec00020	2	1	-3	2
Pentose phosphate pathway	ec00030	3	2	-5	3
Fructose and mannose metabolism	ec00051	-1	1	-7	5
Fatty acid metabolism	ec00071	-1	-1	-3	-2
Alanine, aspartate and glutamate metabolism	ec00250	9	6	-12	1
Glycine, serine and threonine metabolism	ec00260	3	-1	-6	2
Cysteine and methionine metabolism	ec00270	3	1	-3	0
Valine, leucine and isoleucine degradation	ec00280	-2	-2	-4	-2
Arginine and proline metabolism	ec00330	8	5	-3	3
Phenylalanine, tyrosine and tryptophan biosynthesis	ec00400	3	3	-2	0
Cyanoamino acid metabolism	ec00460	1	1	-4	1
Starch and sucrose metabolism	ec00500	3	2	-2	1
Other glycan degradation	ec00511	5	1	1	1
Various types of N-glycan biosynthesis	ec00513	1	1	1	0
Amino sugar and nucleotide sugar metabolism	ec00520	7	7	-2	4
Glyoxylate and dicarboxylate metabolism	ec00630	0	-3	-7	-3
One carbon pool by folate	ec00670	1	-1	-2	-2
Carbon fixation pathways in prokaryotes	ec00720	0	1	-6	1
Vitamin B6 metabolism	ec00750	1	1	1	1
Isoquinoline alkaloid biosynthesis	ec00950	1	1	0	-1
Tropane, piperidine and pyridine alkaloid biosynthesis	ec00960	1	1	0	-1
Drug metabolism - other enzymes	ec00983	2	0	-1	0
Oxidative phosphorylation	ec00190	1	3	0	2
Histidine metabolism	ec00340	1	-1	-1	0
D-Alanine metabolism	ec00473	1	1	-1	1
Lipopolysaccharide biosynthesis	ec00540	0	0	-2	1
Glycerolipid metabolism	ec00561	0	1	-2	-1
Biotin metabolism	ec00780	1	1	-1	1
Retinol metabolism	ec00830	1	1	-1	0
Galactose metabolism	ec00052	1	0	2	-1
Tyrosine metabolism	ec00350	2	2	-1	-1
Glycosaminoglycan degradation	ec00531	2	0	2	-1
Sphingolipid metabolism	ec00600	1	-2	-1	-2
Riboflavin metabolism	ec00740	2	2	-2	2
Lysine biosynthesis	ec00300	2	0	-2	2
Glutathione metabolism	ec00480	3	4	-2	2
Purine metabolism	ec00230	-2	-4	-7	-4
Pyrimidine metabolism	ec00240	1	2	-6	-2
Nitrogen metabolism	ec00910	6	6	-9	3
Inositol phosphate metabolism	ec00562	-1	0	-2	0
Taurine and hypotaurine metabolism	ec00430	-1	-2	-4	-1
Valine, leucine and isoleucine biosynthesis	ec00290	-1	-2	-2	-1

Table S5. Relative changes in selected pathways referred to FS-0. The changes in each pathway have been estimated by pooling the changes in all the enzymes (characterized by their EC codes) assigned to the corresponding pathway. Data refer to samples from patient P1.

Kegg ID	KEGG metabolism/pathway	Fold change in expression of proteins assigned to KEGG metabolism/pathway			
		FS-3 vs FS0	FS-6 vs FS0	FS-11 vs FS0	FS-14 vs FS0
	Carbohydrate metabolism				
ec00010	Glycolysis / Gluconeogenesis	3.701	5.411	-32.232	3.290
ec00020	Citrate cycle (TCA cycle)	54.715	42.290	-4.508	52.389
ec00030	Pentose phosphate pathway	3.693	7.828	-17.839	7.778
ec00040	Pentose and glucuronate interconversions	0.433	1.121	-9.139	1.958
	Energy metabolism				
ec00190	Oxidative phosphorylation	22.676	24.426	-3.278	23.486
	Nucleotide metabolism				
ec00230	Purine metabolism	30.566	22.206	-40.882	23.132
ec00240	Pyrimidine metabolism	29.593	30.369	-65.126	18.793
	Amino acid metabolism				
ec00250	Alanine, aspartate and glutamate metabolism	22.223	16.990	-117.436	5.145
ec00260	Glycine, serine and threonine metabolism	0.275	-3.544	-26.805	-3.516
ec00270	Cysteine and methionine metabolism	26.133	2.501	-0.559	-5.523
ec00290	Valine, leucine and isoleucine biosynthesis	-0.416	-4.307	-13.557	1.961
ec00300	Lysine biosynthesis	22.215	18.723	0.822	19.770
ec00330	Arginine and proline metabolism	23.467	18.151	-2.652	13.455
ec00340	Histidine metabolism	3.876	-0.913	-24.986	1.723
ec00350	Tyrosine metabolism	5.644	6.940	-1.580	-2.206
ec00360	Phenylalanine metabolism	3.458	4.273	1.020	-1.858
ec00380	Tryptophan metabolism	-16.417	-18.035	-18.360	8.528
ec00400	Phenylalanine, tyrosine and tryptophan biosynthesis	8.478	7.169	-3.403	-0.463

Glycan Biosynthesis and Metabolism
Other types of O-glycan biosynthesis
N-Glycan biosynthesis
Various types of N-glycan biosynthesis
Mucin type O-glycan biosynthesis
Glycosphingolipid biosynthesis - globoseries
Glycosaminoglycan biosynthesis - chondroitin sulfate
Glycosphingolipid biosynthesis - lact and neolacto series
Other glycan degradation
[B] Glycosyltransferases
Glycosaminoglycan biosynthesis - heparan sulfate
Glycosaminoglycan degradation
Galactose metabolism
Glycosylphosphatidylinositol (GPI)-anchor biosynthesis
[B] Proteoglycans
Glycosphingolipid biosynthesis - ganglioseries
Glycosaminoglycan biosynthesis - keratan sulfate
alpha-Linolenic acid metabolism
Linoleic acid metabolism
Arachidonic acid metabolism
Phenylpropanoid biosynthesis
[B] Lipids
Biosynthesis of unsaturated fatty acids
Glycerolipid metabolism
Lipid Metabolism
[B] Phytochemical compounds
Isoflavonoid biosynthesis
[B] Lipids biosynthesis proteins
Cutin, suberine and wax biosynthesis
Sphingolipid metabolism
Ether lipid metabolism
Inositol phosphate metabolism
Fatty acid biosynthesis
Fatty acid metabolism
Flavonoid biosynthesis
Carotenoid biosynthesis
Retinol metabolism
Flavone and flavonol biosynthesis
Anthocyanin biosynthesis
Limonene and pinene degradation
Zeatin biosynthesis
Monoterpenoid biosynthesis
Sesquiterpenoid biosynthesis
Terpenoid backbone biosynthesis
Lipoic acid metabolism
Chloroalkane and chloroalkene degradation
Steroid biosynthesis
Insect hormone biosynthesis
Primary bile acid biosynthesis
Caprolactam degradation
Atrazine degradation
Methane metabolism
Steroid hormone biosynthesis
Diterpenoid biosynthesis
Naphthalene degradation
Aminobenzoate degradation
Dioxin degradation
Xylene degradation
Fluorobenzoate degradation
Metabolism of Terpenoids and Polyketides
Secondary bile acid biosynthesis
Brassinosteroid biosynthesis
Benzoate degradation
Toluene degradation
Ethylbenzene degradation
Nitrotoluene degradation
Polycyclic aromatic hydrocarbon degradation
[B] Cytochrome P450
Xenobiotics Biodegradation and Metabolism
Metabolism of xenobiotics by cytochrom P450
Drug metabolism - cytochrom P450
Drug metabolism - other enzymes
Peptidoglycan biosynthesis
Biosynthesis of type II polyketide products
Biosynthesis of type II polyketide backbone
Butanoate metabolism
Fatty acid elongation in mitochondria
Reductive carboxylate cycle (CO2 fixation)
Carbon fixation
Citrate cycle (TCA cycle)
Glyoxylate and dicarboxylate metabolism
Methane metabolism
Carbohydrate Metabolism
Glycolysis / Gluconeogenesis
Pyruvate metabolism
Propanoate metabolism
C5-Branched dibasic acid metabolism
Oxidative phosphorylation
DDT degradation
Lipopolysaccharide biosynthesis
Streptomycin biosynthesis
Butirosin and neomycin biosynthesis
Biosynthesis of ansamycins
Starch and sucrose metabolism
Polyketide sugar unit biosynthesis
Amino sugar and nucleotide sugar metabolism
Pentose phosphate metabolism
Fructose and mannose metabolism
Biosynthesis of 12-, 14- and 16-membered macrolides
Photosynthesis - antenna proteins
Photosynthesis
[B] Photosynthesis proteins
Energy Metabolism
Phosphonate and phosphinate metabolism
D-Alanine metabolism
Selenocompound metabolism
Lysine degradation
Synthesis and degradation of Ketone bodies
Cyanoamino acid metabolism
Alanine , aspartate and glutamate metabolism
Lysine biosynthesis
Tetracycline biosynthesis
Chlorocyclohexane and chlorobenzene degradation
Styrene degradation
Bisphenol degradation
Penicillin and cephalosporin biosynthesis
Amino Acid Metabolism
Puromycin biosynthesis
Purine metabolism
Ascorbate and aldarate metabolism
Pentose and glucuronate interconversions
Nucleotide Metabolism
Pyrimidine metabolism
Biosynthesis of vancomycin group antibiotics
Phenylalanine metabolism
Novobiocin biosynthesis
Sulfur metabolism
Biosynthesis of siderophore group nonribosomal peptides
Histidine metabolism
Glycine, serine and threonine metabolism
Cysteine and methionine metabolism
Glutathione metabolism
D-Glutamine and D-glutamate metabolism
beta-Lactam resistance
Metabolism of Other Amino Acid
beta-Alanine metabolism
Caffeine metabolism
Riboflavin metabolism
Tyrosine metabolism
Phenylalanine , tyrosine and tryptophan biosynthesis
Taurine and hypotaurine metabolism
Tryptophan metabolism
Benzoxazinone biosynthesis
Valine, leucine and isoleucine biosynthesis
Valine, leucine and isoleucine degradation
Nitrogen metabolism
Glucosinolate biosynthesis
Arginine and proline metabolism
Tropane, piperidine and pyridine alkaloid biosynthesis
Biotin metabolism
Thiamine metabolism
Metabolism of Cofactors and Vitamins
Folate biosynthesis
Vitamin B6 metabolism
One carbon pool by folate
Isoquinoline alkaloid biosynthesis
Biosynthesis of Other Secondary Metabolites
Acridone alkaloid biosynthesis
Indole alkaloid biosynthesis
Ubiquinone and other terpenoid-quinone biosynthesis
Pantothenate and CoA biosynthesis
Porphyrin and chlorophyll metabolism
Clavulanic acid biosynthesis
D-Arginine and D-ornithine metabolism
Nicotinate and nicotinamide metabolism


Glycan Biosynthesis and Metabolism
Other types of O-glycan biosynthesis
N-Glycan biosynthesis
Various types of N-glycan biosynthesis
Mucin type O-glycan biosynthesis
Glycosphingolipid biosynthesis - globoseries
Glycosaminoglycan biosynthesis - chondroitin sulfate
Glycosphingolipid biosynthesis - lact and neolacto series
Other glycan degradation
[B] Glycosyltransferases
Glycosaminoglycan biosynthesis - heparan sulfate
Starch and sucrose metabolism
Glycosaminoglycan degradation
Galactose metabolism
Glycosylphosphatidylinositol (GPI)-anchor biosynthesis
[B] Proteoglycans
Glycosphingolipid biosynthesis - ganglioseries
Glycosaminoglycan biosynthesis - keratan sulfate
alpha-Linolenic acid metabolism
Amino sugar and nucleotide sugar metabolism
Fructose and mannose metabolism
Glycerophospholipid metabolism
Linoleic acid metabolism
Arachidonic acid metabolism
Phenylpropanoid biosynthesis
[B] Lipids
Biosynthesis of unsaturated fatty acids
Glycerolipid metabolism
Lipid Metabolism
[B] Phytochemical compounds
Isoflavonoid biosynthesis
[B] Lipids biosynthesis proteins
Cutin, suberine and wax biosynthesis
Sphingolipid metabolism
Ether lipid metabolism
Inositol phosphate metabolism
Carbohydrate Metabolism
Glycolysis / Gluconeogenesis
Fatty acid biosynthesis
Peptidoglycan biosynthesis
Flavonoid biosynthesis
Carotenoid biosynthesis
Fatty acid metabolism
Biosynthesis of type II polyketide products
Retinol metabolism
Pyruvate metabolism
Flavone and flavonol biosynthesis
Anthocyanin biosynthesis
Limonene and pinene degradation
Zeatin biosynthesis
Biosynthesis of type II polyketide backbone
Monoterpenoid biosynthesis
Butanoate metabolism
Fatty acid elongation in mitochondria
Sesquiterpenoid biosynthesis
Lipoic acid metabolism
Chloroalkane and chloroalkene degradation
Reductive carboxylate cycle (CO2 fixation)
Terpenoid backbone biosynthesis
Caprolactam degradation
Carbon fixation
Steroid biosynthesis
Insect hormone biosynthesis
Primary bile acid biosynthesis
Atrazine degradation
Methane metabolism
Citrate cycle (TCA cycle)
Glyoxylate and dicarboxylate metabolism
Alanine , aspartate and glutamate metabolism
Steroid hormone biosynthesis
Diterpenoid biosynthesis
Naphthalene degradation
Aminobenzoate degradation
Dioxin degradation
Xylene degradation
Fluorobenzoate degradation
Metabolism of Terpenoids and Polyketides
Secondary bile acid biosynthesis
Brassinosteroid biosynthesis
Benzoate degradation
Toluene degradation
Ethylbenzene degradation
Nitrotoluene degradation
Polycyclic aromatic hydrocarbon degradation
[B] Cytochrome P450
Xenobiotics Biodegradation and Metabolism
Metabolism of xenobiotics by cytochrom P450
Drug metabolism - cytochrom P450
Drug metabolism - other enzymes
Lipopolysaccharide biosynthesis
Streptomycin biosynthesis
Butirosin and neomycin biosynthesis
Biosynthesis of ansamycins
Puromycin biosynthesis
Purine metabolism
Ascorbate and aldarate metabolism
Polyketide sugar unit biosynthesis
Pentose and glucuronate interconversions
Pentose phosphate metabolism
Biosynthesis of 12-, 14- and 16-membered macrolides
Photosynthesis - antenna proteins
Amino Acid Metabolism
Photosynthesis
[B] Photosynthesis proteins
Energy Metabolism
Sulfur metabolism
Biosynthesis of siderophore group nonribosomal peptides
Phosphonate and phosphinate metabolism
D-Alanine metabolism
Histidine metabolism
Glycine, serine and threonine metabolism
Synthesis and degradation of Ketone bodies
Selenocompound metabolism
Cyanoamino acid metabolism
Propanoate metabolism
Lysine degradation
Lysine biosynthesis
C5-Branched dibasic acid metabolism
Tetracycline biosynthesis
Cysteine and methionine metabolism
Chlorocyclohexane and chlorobenzene degradation
Bisphenol degradation
Styrene degradation
Oxidative phosphorylation
DDT degradation
Penicillin and cephalosporin biosynthesis
Glutathione metabolism
beta-Lactam resistance
Nucleotide Metabolism
Metabolism of Cofactors and Vitamins
Thiamine metabolism
Caffeine metabolism
beta-Alanine metabolism
Riboflavin metabolism
Folate biosynthesis
Pyrimidine metabolism
Vitamin B6 metabolism
Tyrosine metabolism
Biosynthesis of vancomycin group antibiotics
Phenylalanine , tyrosine and tryptophan biosynthesis
Phenylalanine metabolism
One carbon pool by folate
Isoquinoline alkaloid biosynthesis
Novobiocin biosynthesis
Biosynthesis of Other Secondary Metabolites
Acridone alkaloid biosynthesis
Taurine and hypotaurine metabolism
Indole alkaloid biosynthesis
Tryptophan metabolism
Ubiquinone and other terpenoid-quinone biosynthesis
Benzoxazinone biosynthesis
Pantothenate and CoA biosynthesis
Porphyrin and chlorophyll metabolism
Valine, leucine and isoleucine biosynthesis
Clavulanic acid biosynthesis
Valine, leucine and isoleucine degradation
Nitrogen metabolism
D-Arginine and D-ornithine metabolism
Glucosinolate biosynthesis
Arginine and proline metabolism
Nicotinate and nicotinamide metabolism
Tropane, piperidine and pyridine alkaloid biosynthesis
D-Glutamine and D-glutamate metabolism
Biotin metabolism
Metabolism of Other Amino Acid


Glycan Biosynthesis and Metabolism
Glycosphingolipid biosynthesis - lact and neolacto series
[B] Glycosyltransferases
Glycosphingolipid biosynthesis - globoseries
N-Glycan biosynthesis
Other types of O-glycan biosynthesis
Other glycan degradation
Various types of N-glycan biosynthesis
Mucin type O-glycan biosynthesis
Glycosaminoglycan biosynthesis - chondroitin sulfate
Glycosaminoglycan biosynthesis - heparan sulfate
Glycosaminoglycan degradation
Starch and sucrose metabolism
Galactose metabolism
Glycosylphosphatidylinositol (GPI)-anchor biosynthesis
alpha-Linolenic acid metabolism
Glycosaminoglycan biosynthesis - keratan sulfate
Glycosphingolipid biosynthesis - ganglioseries
[B] Proteoglycans
Lipopolysaccharide biosynthesis
Streptomycin biosynthesis
Butirosin and neomycin biosynthesis
Biosynthesis of ansamycins
Polyketide sugar unit biosynthesis
Amino sugar and nucleotide sugar metabolism
Fructose and mannose metabolism
Pentose phosphate metabolism
Glycerophospholipid metabolism
Linoleic acid metabolism
Arachidonic acid metabolism
Biosynthesis of unsaturated fatty acids
Glycerolipid metabolism
Ether lipid metabolism
Inositol phosphate metabolism
Sphingolipid metabolism
[B] Lipids
Lipid Metabolism
[B] Lipids biosynthesis proteins
Cutin, suberine and wax biosynthesis
Fatty acid biosynthesis
Fatty acid metabolism
Peptidoglycan biosynthesis
Biosynthesis of type II polyketide products
Biosynthesis of type II polyketide backbone
Butanoate metabolism
Fatty acid elongation in mitochondria
Propanoate metabolism
Lysine degradation
Reductive carboxylate cycle (CO2 fixation)
Carbon fixation
Citrate cycle (TCA cycle)
Glyoxylate and dicarboxylate metabolism
C5-Branched dibasic acid metabolism
Alanine , aspartate and glutamate metabolism
Carbohydrate Metabolism
Glycolysis / Gluconeogenesis
Pyruvate metabolism
Photosynthesis - antenna proteins
Photosynthesis
[B] Photosynthesis proteins
Oxidative phosphorylation
Energy Metabolism
Amino Acid Metabolism
Phosphonate and phosphinate metabolism
D-Alanine metabolism
Selenocompound metabolism
Synthesis and degradation of ketone bodies
Cyanoamino acid metabolism
Glycine, serine and threonine metabolism
Histidine metabolism
Lysine biosynthesis
Cysteine and methionine metabolism
Sulfur metabolism
Biosynthesis of siderophore group nonribosomal peptides
Penicillin and cephalosporin biosynthesis
beta-Lactam resistance
Glutathione metabolism
Tryptophan metabolism
Taurine and hypotaurine metabolism
Benzoxazinone biosynthesis
Valine, leucine and isoleucine biosynthesis
Valine, leucine and isoleucine degradation
Nitrogen metabolism
Arginine and proline metabolism
Glucosinolate biosynthesis
Tropane, piperidine and pyridine alkaloid biosynthesis
D-Glutamine and D-glutamate metabolism
Biotin metabolism
D-Arginine and D-ornithine metabolism
Nicotinate and nicotinamide metabolism
Porphyrin and chlorophyll metabolism
Clavulanic acid biosynthesis
Pantothenate and CoA biosynthesis
Ubiquinone and other terpenoid-quinone biosynthesis
Indole alkaloid biosynthesis
Acridone alkaloid biosynthesis
Isoquinoline alkaloid biosynthesis
Phenylalanine , tyrosine and tryptophan biosynthesis
Phenylalanine metabolism
Tyrosine metabolism
beta-Alanine metabolism
Caffeine metabolism
Riboflavin metabolism
Folate biosynthesis
Vitamin B6 metabolism
Thiamine metabolism
One carbon pool by folate
Metabolism of Cofactors and Vitamins
Nucleotide Metabolism
Purine metabolism
Pyrimidine metabolism
Puromycin biosynthesis
Pentose and glucuronate interconversions
Ascorbate and aldarate metabolism
Biosynthesis of vancomycin group antibiotics
Novobiocin biosynthesis
Biosynthesis of Other Secondary Metabolites
Metabolism of Other Amino Acid
Chloroalkane and chloroalkene degradation
Chlorocyclohexane and chlorobenzene degradation
Styrene degradation
Bisphenol degradation
DDT degradation
Ethylbenzene degradation
Toluene degradation
Benzoate degradation
Xylene degradation
Dioxin degradation
Aminobenzoate degradation
Naphthalene degradation
Atrazine degradation
Methane metabolism
Caprolactam degradation
Fluorobenzoate degradation
Nitrotoluene degradation
Polycyclic aromatic hydrocarbon degradation
Tetracycline biosynthesis
Steroid biosynthesis
Steroid hormone biosynthesis
Primary bile acid biosynthesis
Secondary bile acid biosynthesis
Terpenoid backbone biosynthesis
Sesquiterpenoid biosynthesis
Monoterpenoid biosynthesis
Diterpenoid biosynthesis
Limonene and pinene degradation
Zeatin biosynthesis
Retinol metabolism
Carotenoid biosynthesis
Flavonoid biosynthesis
Flavone and flavonol biosynthesis
Anthocyanin biosynthesis
Isoflavonoid biosynthesis
Phenylpropanoid biosynthesis
[B] Phytochemical compounds
Brassinosteroid biosynthesis
Insect hormone biosynthesis
[B] Cytochrome P450
Metabolism of Terpenoids and Polyketides
Xenobiotics Biodegradation and Metabolism
Metabolism of xenobiotics by cytochrom P450
Drug metabolism - cytochrom P450
Drug metabolism - other enzymes

Glycan Biosynthesis and Metabolism
Other types of O-glycan biosynthesis
N-Glycan biosynthesis
Various types of N-glycan biosynthesis
Mucin type O-glycan biosynthesis
Glycosphingolipid biosynthesis - globoseries
Glycosaminoglycan biosynthesis - chondroitin sulfate
Lipopolysaccharide biosynthesis
Butirosin and neomycin biosynthesis
Streptomycin biosynthesis
Glycosphingolipid biosynthesis - lact and neolacto series
Other glycan degradation
[B] Glycosyltransferases
Glycosaminoglycan biosynthesis - heparan sulfate
Biosynthesis of ansamycins
Starch and sucrose metabolism
Glycosaminoglycan degradation
Galactose metabolism
Glycosylphosphatidylinositol (GPI)-anchor biosynthesis
Ascorbate and aldarate metabolism
Nucleotide Metabolism
Puromycin biosynthesis
Purine metabolism
Thiamine metabolism
Metabolism of Cofactors and Vitamins
[B] Proteoglycans
Glycosphingolipid biosynthesis - ganglioseries
Glycosaminoglycan biosynthesis - keratan sulfate
alpha-Linolenic acid metabolism
Polyketide sugar unit biosynthesis
Pentose and glucuronate interconversions
beta-Alanine metabolism
Caffeine metabolism
Riboflavin metabolism
Folate biosynthesis
Pyrimidine metabolism
Biosynthesis of vancomycin group antibiotics
Tyrosine metabolism
Vitamin B6 metabolism
Amino sugar and nucleotide sugar metabolism
Fructose and mannose metabolism
Pentose phosphate metabolism
Biosynthesis of 12-, 14- and 16-membered macrolides
Phenylalanine , tyrosine and tryptophan biosynthesis
One carbon pool by folate
Glycerophospholipid metabolism
Linoleic acid metabolism
Arachidonic acid metabolism
Phenylalanine metabolism
Isoquinoline alkaloid biosynthesis
Photosynthesis - antenna proteins
Novobiocin biosynthesis
Biosynthesis of Other Secondary Metabolites
Phenylpropanoid biosynthesis
[B] Lipids
Biosynthesis of unsaturated fatty acids
Glycerolipid metabolism
[B] Phytochemical compounds
Lipid Metabolism
Carbohydrate Metabolism
Amino Acid Metabolism
Acridone alkaloid biosynthesis
Ether lipid metabolism
Photosynthesis
Isoflavonoid biosynthesis
[B] Lipids biosynthesis proteins
Cutin, suberine and wax biosynthesis
Sphingolipid metabolism
Inositol phosphate metabolism
Glycolysis / Gluconeogenesis
[B] Photosynthesis proteins
Sulfur metabolism
Taurine and hypotaurine metabolism
Indole alkaloid biosynthesis
Biosynthesis of siderophore group nonribosomal peptides
Energy Metabolism
Fatty acid biosynthesis
Peptidoglycan biosynthesis
Tryptophan metabolism
Flavonoid biosynthesis
Carotenoid biosynthesis
Fatty acid metabolism
Biosynthesis of type II polyketide products
Phosphonate and phosphinate metabolism
Histidine metabolism
Ubiquinone and other terpenoid-quinone biosynthesis
Retinol metabolism
D-Alanine metabolism
Pyruvate metabolism
Benzoxazinone biosynthesis
Flavone and flavonol biosynthesis
Anthocyanin biosynthesis
Glycine, serine and threonine metabolism
Valine, leucine and isoleucine biosynthesis
Pantothenate and CoA biosynthesis
Limonene and pinene degradation
Zeatin biosynthesis
Biosynthesis of type II polyketide backbone
Synthesis and degradation of Ketone bodies
Selenocompound metabolism
Cyanoamino acid metabolism
Porphyrin and chlorophyll metabolism
Monoterpenoid biosynthesis
Butanoate metabolism
Fatty acid elongation in mitochondria
Propanoate metabolism
Lysine degradation
Clavulanic acid biosynthesis
Sesquiterpenoid biosynthesis
Lipoic acid metabolism
Chloroalkane and chloroalkene degradation
Reductive carboxylate cycle (CO2 fixation)
Valine, leucine and isoleucine degradation
Terpenoid backbone biosynthesis
Caprolactam degradation
Carbon fixation
C5-Branched dibasic acid metabolism
Lysine biosynthesis
Cysteine and methionine metabolism
Nitrogen metabolism
Steroid biosynthesis
Citrate cycle (TCA cycle)
Insect hormone biosynthesis
Primary bile acid biosynthesis
Atrazine degradation
Methane metabolism
Alanine , aspartate and glutamate metabolism
D-Arginine and D-ornithine metabolism
Glyoxylate and dicarboxylate metabolism
Steroid hormone biosynthesis
Tetracycline biosynthesis
Glucosinolate biosynthesis
Diterpenoid biosynthesis
Aminobenzoate degradation
Naphthalene degradation
Dioxin degradation
Arginine and proline metabolism
Nicotinate and nicotinamide metabolism
Xylene degradation
Chlorocyclohexane and chlorobenzene degradation
Metabolism of Terpenoids and Polyketides
Fluorobenzoate degradation
Bisphenol degradation
Glutathione metabolism
Styrene degradation
Tropane, piperidine and pyridine alkaloid biosynthesis
Secondary bile acid biosynthesis
Oxidative phosphorylation
Penicillin and cephalosporin biosynthesis
D-Glutamine and D-glutamate metabolism
Biotin metabolism
Brassinosteroid biosynthesis
Benzoate degradation
Toluene degradation
Ethylbenzene degradation
DDT degradation
beta-Lactam resistance
Metabolism of Other Amino Acid
[B] Cytochrome P450
Polycyclic aromatic hydrocarbon degradation
Nitrotoluene degradation
Xenobiotics Biodegradation and Metabolism
Metabolism of xenobiotics by cytochrom P450
Drug metabolism - cytochrom P450
Drug metabolism - other enzymes

Glycan Biosynthesis and Metabolism
Glycosphingolipid biosynthesis - lact and neolacto series
[B] Glycosyltransferases
Glycosphingolipid biosynthesis - globoseries
N-Glycan biosynthesis
Other types of O-glycan biosynthesis
Other glycan degradation
Various types of N-glycan biosynthesis
Mucin type O-glycan biosynthesis
Glycosaminoglycan biosynthesis - chondroitin sulfate
Glycosaminoglycan biosynthesis - heparan sulfate
Glycosaminoglycan degradation
Glycosphingolipid biosynthesis - ganglioseries
Glycosaminoglycan biosynthesis - keratan sulfate
[B] Proteoglycans
Lipopolysaccharide biosynthesis
Streptomycin biosynthesis
Butirosin and neomycin biosynthesis
Biosynthesis of ansamycins
Starch and sucrose metabolism
Galactose metabolism
Glycosylphosphatidylinositol (GPI)-anchor biosynthesis
alpha-Linolenic acid metabolism
Polyketide sugar unit biosynthesis
Amino sugar and nucleotide sugar metabolism
Fructose and mannose metabolism
Pentose phosphate metabolism
Pentose and glucuronate interconversions
Biosynthesis of 12-, 14- and 16-membered macrolides
Photosynthesis - antenna proteins
Linoleic acid metabolism
Arachidonic acid metabolism
Glycerophospholipid metabolism
Phenylpropanoid biosynthesis
[B] Lipids
Biosynthesis of unsaturated fatty acids
Glycerolipid metabolism
Lipid Metabolism
Carbohydrate Metabolism
Amino Acid Metabolism
Energy Metabolism
Nucleotide Metabolism
Metabolism of Cofactors and Vitamins
Biosynthesis of Other Secondary Metabolites
Metabolism of Terpenoids and Polyketides
Xenobiotics Biodegradation and Metabolism
Metabolism of Other Amino Acid
[B] Phytochemical compounds
Isoflavonoid biosynthesis
Flavonoid biosynthesis
Carotenoid biosynthesis
Retinol metabolism
Flavone and flavonol biosynthesis
Anthocyanin biosynthesis
Limonene and pinene degradation
Zeatin biosynthesis
Monoterpenoid biosynthesis
Sesquiterpenoid biosynthesis
Terpenoid backbone biosynthesis
Insect hormone biosynthesis
Diterpenoid biosynthesis
Brassinosteroid biosynthesis
Secondary bile acid biosynthesis
[B] Cytochrome P450
Polycyclic aromatic hydrocarbon degradation
[B] Lipids biosynthesis proteins
Cutin, suberine and wax biosynthesis
Sphingolipid metabolism
Ether lipid metabolism
Inositol phosphate metabolism
Fatty acid biosynthesis
Fatty acid metabolism
Peptidoglycan biosynthesis
Biosynthesis of type II polyketide products
Biosynthesis of type II polyketide backbone
Butanoate metabolism
Fatty acid elongation in mitochondria
Lipoic acid metabolism
Chloroalkane and chloroalkene degradation
Reductive carboxylate cycle (CO2 fixation)
Caprolactam degradation
Steroid biosynthesis
Primary bile acid biosynthesis
Atrazine degradation
Methane metabolism
Steroid hormone biosynthesis
Naphthalene degradation
Aminobenzoate degradation
Dioxin degradation
Xylene degradation
Fluorobenzoate degradation
Benzoate degradation
Toluene degradation
Nitrotoluene degradation
Ethylbenzene degradation
Drug metabolism - cytochrom P450
Drug metabolism - other enzymes
Metabolism of xenobiotics by cytochrom P450
Glycolysis / Gluconeogenesis
Carbon fixation
Citrate cycle (TCA cycle)
Glyoxylate and dicarboxylate metabolism
Pyruvate metabolism
Photosynthesis
[B] Photosynthesis proteins
Phosphonate and phosphinate metabolism
D-Alanine metabolism
Oxidative phosphorylation
C5-Branched dibasic acid metabolism
Alanine , aspartate and glutamate metabolism
Lysine biosynthesis
Propanoate metabolism
Lysine degradation
Synthesis and degradation of Ketone bodies
Selenocompound metabolism
Cyanoamino acid metabolism
Tetracycline biosynthesis
Chlorocyclohexane and chlorobenzene degradation
Styrene degradation
Bisphenol degradation
Penicillin and cephalosporin biosynthesis
DDT degradation
beta-Lactam resistance
Puromycin biosynthesis
Purine metabolism
Ascorbate and aldarate metabolism
Pyrimidine metabolism
Biosynthesis of vancomycin group antibiotics
Novobiocin biosynthesis
Phenylalanine metabolism
Sulfur metabolism
Biosynthesis of siderophore group nonribosomal peptides
Histidine metabolism
Glycine, serine and threonine metabolism
Cysteine and methionine metabolism
Valine, leucine and isoleucine biosynthesis
Valine, leucine and isoleucine degradation
Nitrogen metabolism
Glucosinolate biosynthesis
Arginine and proline metabolism
Glutathione metabolism
D-Glutamine and D-glutamate metabolism
Thiamine metabolism
Caffeine metabolism
beta-Alanine metabolism
Riboflavin metabolism
Folate biosynthesis
Vitamin B6 metabolism
Tyrosine metabolism
Phenylalanine , tyrosine and tryptophan biosynthesis
One carbon pool by folate
Isoquinoline alkaloid biosynthesis
Acridone alkaloid biosynthesis
Taurine and hypotaurine metabolism
Tryptophan metabolism
Benzoxazinone biosynthesis
Indole alkaloid biosynthesis
Ubiquinone and other terpenoid-quinone biosynthesis
Pantothenate and CoA biosynthesis
Porphyrin and chlorophyll metabolism
Clavulanic acid biosynthesis
D-Arginine and D-ornithine metabolism
Nicotinate and nicotinamide metabolism
Tropane, piperidine and pyridine alkaloid biosynthesis
Biotin metabolism